

### AMENDMENTS TO THE CLAIMS

1. (Currently Amended) ~~Suspension~~ A suspension of microcapsules in an aqueous liquid phase that allows ~~[[the]]~~ modified release of at least one active principle (~~excluding amoxicillin~~) and is intended for oral administration, ~~wherein said suspension characterized in that: [[■ it]]~~ comprises a plurality of microcapsules and an aqueous liquid phase, wherein the aqueous liquid phase is saturated or becomes saturated with active principle(s) on contact with the microcapsules, and wherein each microcapsule comprises consisting of

(a) a core containing comprising at least one active principle(s), wherein none of the at least one active principle(s) is amoxicillin (excluding amoxicillin) and [[of]]

(b) a film coating that: [[•]] (i) is applied to the core, [[•]] (ii) controls the modified release of the active principle(s) in gastrointestinal tract fluids, [[•]] and (iii) comprises has a composition corresponding to one of the following three families A, B and C:

[[⇒]] Family A

[[♦1A --]] (1) at least one film-forming polymer (P1) insoluble in [[the]] gastrointestinal tract fluids, present in an amount of 50 to 90 and preferably of 50 to 80 % by dry weight[[,]] based on the total weight of the coating composition, and consisting of wherein at least one of said at least one film-forming polymer (P1) is a at least one water-insoluble cellulose derivative;

[[♦2A --]] (2) at least one nitrogen-containing polymer (P2) present in an amount of 2 to 25 and preferably of 5 to 15 % by dry weight[[,]] based on the total weight of the coating composition, and consisting of wherein at least one of said at least one nitrogen-containing polymer (P2) is selected from the group consisting of: at least one polyacrylamide, and/or poly-N-vinylamide, and [[/ or]] poly-N-vinylactam;

[[♦3A --]] (3) at least one plasticizer present in an amount of 2 to 20 and preferably of 4 to 15 % by dry weight[[,]] based on the total weight of the coating composition, and consisting of at least one of the following compounds: wherein at least one of said at least one plasticizer is selected from the group consisting of: glycerol esters, phthalates, citrates, sebacates, cetyl alcohol esters, and castor oil; and

[[♦4A --]] (4) at least one surfactant [[and/]] or lubricant present in an amount of 2 to 20 and preferably of 4 to 15 % by dry weight[[,]] based on the total weight of the coating composition, and wherein at least one of said at least one surfactant or lubricant is selected from the group consisting of: anionic surfactants, and/or non-ionic surfactants, and [[/ or]] lubricants,

and mixtures thereof ~~it being possible for said agent to comprise only one or a mixture of the above mentioned products;~~

[[⊃]] Family B

[[~]]1B—at least one hydrophilic polymer carrying groups ionized at neutral pH and preferably selected from cellulose derivatives;

[[~]]2B—at least one hydrophobic compound different from A;

[[⊃]] Family C

[[♦]]1C—at least one film-forming polymer insoluble in [[the]] gastrointestinal tract fluids;

[[♦]]2C—at least one water-soluble polymer;

[[♦]]3C—at least one plasticizer;

[[♦]]4C—optionally at least one surfactant / lubricant preferably selected from the following group of products: [[~]]anionic surfactants; [[~]]and/or non-ionic surfactants; [[■]] and the liquid phase is saturated or becomes saturated with active principle(s) on contact with the microcapsules.

2. (Currently Amended) The suspension Suspension according to claim 1, wherein characterized in that the families A, B and C from which the constituents of the coating composition are selected are as follows:

[[⊃]] Family A

[[♦1A --]] at least one of the at least one film-forming polymer (P1) is selected from the group consisting of ethyl cellulose and [[/or]] cellulose acetate;

[[♦2A --]] at least one of the at least one nitrogen-containing polymer (P2) is selected from the group consisting of polyacrylamide and [[/or]] polyvinylpyrrolidone;

[[♦3A --]] at least one of the at least one plasticizer is castor oil;

[[♦4A --]] at least one of the at least one surfactant or lubricant is selected from the group consisting of: an alkali metal ~~or~~ alkaline earth metal salt of fatty acids, an alkaline earth metal salt of fatty acids, stearic acid, and/or oleic acid being preferred, a polyethoxylated sorbitan ester, a polyethoxylated castor oil derivative, a stearate, preferably calcium, magnesium, aluminium or zinc stearate, a stearyl fumarate, preferably sodium stearyl fumarate, [[or]] glycerol behenate, taken individually or in a mixture with one another; and mixtures thereof.

[[⇔]] **Family-B**

[[♦]]1B

[[~]]cellulose acetate-phthalate;

[[~]]hydroxypropyl-methyl-cellulose-phthalate;

[[~]]hydroxypropyl-methyl-cellulose acetate-succinate;

[[~]]-(meth)acrylic acid/(meth)acrylic acid-alkyl (methyl) ester-copolymer;

[[~]]and mixtures thereof;

[[♦]]2B

[[~]]hydrogenated vegetable waxes;

[[~]]triglycerides;

[[~]]animal and vegetable fats (beeswax, carnauba wax, etc.);

[[~]]and mixtures thereof.

[[⇔]] **Family-C**

[[♦]]1C

[[~]]water-insoluble cellulose derivatives, ethyl-cellulose and/or cellulose acetate being particularly preferred;

[[~]]acrylic derivatives;

[[~]]polyvinyl acetates;

[[~]]and mixtures thereof;

[[♦]]2C

[[~]]water-soluble cellulose derivatives;

[[~]]polyacrylamides;

[[~]]poly-N-vinylamides;

[[~]]poly-N-vinylacetams;

[[~]]polyvinyl alcohols (PVA);

[[~]]polyoxyethylenes (POE);

[[~]]polyvinylpyrrolidones (PVP) (the latter being preferred);

[[~]]and mixtures thereof;

[[♦]]3C

[[~]]glycerol and its esters, preferably from the following subgroup: acetylated glycerides, glycerol monostearate, glyceryl triacetate and glycerol-tributyrate;

[[~]]phthalates, preferably from the following subgroup: dibutyl phthalate, diethyl phthalate, dimethyl phthalate and dioctyl phthalate;

[[~]]citrates, preferably from the following subgroup: acetyltributyl citrate, acetyltriethyl citrate, tributyl citrate and triethyl citrate;

[[~]]sebacates, preferably from the following subgroup: diethyl sebacate and dibutyl sebacate;

[[~]]adipates;

[[~]]azelates;

[[~]]benzoates;

[[~]]vegetable oils;

[[~]]fumarates, preferably diethyl fumarate;

[[~]]malates, preferably diethyl malate;

[[~]]oxalates, preferably diethyl oxalate;

[[~]]succinates, preferably dibutyl succinate;

[[~]]butyrates;

[[~]]cetyl alcohol esters;

[[~]]salicylic acid;

[[~]]triacetin;

[[~]]malonates, preferably diethyl malonate;

[[~]]eutin;

[[~]]caster oil (this being particularly preferred);

[[~]]and mixtures thereof;

[[♦]]4C

[[~]]alkali metal or alkaline earth metal salts of fatty acids, stearic and/or oleic acid being preferred;

[[~]]polyethoxylated oils, preferably polyethoxylated hydrogenated castor oil;

polyoxyethylene/polyoxypropylene copolymers;

polyethoxylated sorbitan esters;

polyethoxylated castor oil derivatives;

stearates, preferably calcium, magnesium, aluminium or zinc stearate;

stearylfumarates, preferably sodium stearylfumarate;

~~glycerol behenate;~~  
~~and mixtures thereof.~~

3. (Currently Amended) ~~The suspension~~ Suspension according to claim 1 ~~or 2,~~  
~~characterized in that wherein~~ the film coating consists of a single layer.
4. (Currently Amended) ~~The suspension~~ Suspension according to claim 1, ~~wherein~~  
~~said suspension characterized in that it contains comprises~~ [[: -]] 30 to 95% by weight ~~and~~  
~~preferably 60 to 85% by weight of liquid phase (advantageously water); [[: -]] and 5 to 70% by~~  
~~weight and preferably 15 to 40% by weight of microcapsules.~~
5. (Currently Amended) ~~The suspension~~ Suspension according to claim 1,  
~~characterized in that the amount of solvent liquid phase (preferably water) for the active~~  
~~principle(s) is such that wherein~~ the proportion of dissolved active principle(s) originating from  
the microcapsules is less than or equal to 15% ~~and preferably less than or equal to 5% by weight,~~  
~~based on of~~ the total weight of the active principle(s) contained in the microcapsules.
6. (Cancelled)
7. (Currently Amended) ~~The suspension~~ Suspension according to claim 1 ~~[[6]],~~  
~~characterized in that it is wherein~~ the active principle(s) contained in the microcapsules ~~that~~  
~~saturate saturates~~ the liquid phase.
8. (Currently Amended) ~~The suspension~~ Suspension according to claim 1,  
~~characterized in that it is wherein~~ the aqueous liquid phase is at least partially ~~and preferably~~  
~~totally~~ saturated with active principle(s) by means of non-encapsulated active principle(s) prior  
to the incorporation of the microcapsules into ~~this~~ the aqueous liquid phase.
9. (Currently Amended) ~~The suspension~~ Suspension according to ~~any one of claims~~  
claim 1 to 8, ~~characterized in that wherein~~ the microcapsules have a particle size less than or

equal to 1000 microns, ~~preferably of between 200 and 800 microns and particularly preferably of between 200 and 600 microns.~~

10. (Currently Amended) ~~The suspension~~ Suspension according to ~~any one of claims claim 1 to 9, characterized in that wherein the film coating represents from 1 to 50% and preferably from 5 to 40% of the total weight of the coated microcapsules is film coating.~~

11. (Currently Amended) ~~The suspension~~ Suspension according to claim 10, ~~characterized by having an in vitro release profile obtained using a type II apparatus according to the European Pharmacopoeia 3rd edition, in a phosphate buffer medium of pH 6.8 and at a temperature of 37°C, such that: [[►]] the proportion PI of active principle(s) released during the first 15 minutes of the dissolution test is such that:  $PI \leq 15$  preferably  $PI \leq 5$ ; and [[►]] the remaining active principle(s) is (are) released over a period such that the release time of 50% by weight of AP ( $t_{1/2}$ ) is defined as follows (in hours):  $0.5 \leq t_{1/2} \leq 30$  preferably  $0.5 \leq t_{1/2} \leq 20$ .~~

12. (Currently Amended) ~~The suspension~~ Suspension according to ~~any one of claims claim 1 to 11, characterized in that~~ ~~[: -])~~ wherein the initial *in vitro* release profile  $Pf_i$  obtained just after suspension of the microcapsules in the solvent (preferably aqueous liquid [D]) phase, measured using a type II apparatus according to the European Pharmacopoeia 3rd edition, in a phosphate buffer medium of pH 6.8, at a temperature of 37°C, ~~[[ -]]~~ and the *in vitro* release profile  $Pf_{10}$  obtained 10 days after suspension of the microcapsules in the solvent (preferably aqueous liquid [D]) phase, measured using a type II apparatus according to the European Pharmacopoeia 3rd edition, in a phosphate buffer medium of pH 6.8, at a temperature of 37°C, are similar.

13. (Currently Amended) ~~The suspension~~ Suspension according to ~~any one of claim [[s]] 1 to 12, characterized in that wherein~~ ~~[[its]]~~ the pH of the suspension is arbitrarily acidic or neutral.

14. (Currently Amended) ~~The suspension~~ Suspension according to ~~any one of claim [[s]] 1 characterized in that it wherein the suspension~~ comprises at least one rheology modifier.

15. (Currently Amended) ~~The suspension~~ Suspension according to ~~any one of claim~~ [[s]] 1 to 14 ~~characterized in that it wherein the suspension further~~ comprises at least one agent for modifying the solubility of the active principle(s) in the solvent (preferably aqueous ~~[[I]]~~) liquid phase.

16. (Currently Amended) ~~The suspension~~ Suspension according to ~~any one of claim~~ [[s]] 1 to 15, ~~characterized in that it contains wherein the suspension further comprises~~ at least one additive selected from the group ~~comprising~~ consisting of: surfactants, colourants, dispersants, preservatives, taste improvers, flavourings, sweeteners, antioxidants, and mixtures thereof.

17. (Currently Amended) ~~The suspension~~ Suspension according to ~~any one of claims~~ claim 1 to 16, ~~characterized in that wherein at least one of the at least one active principle(s)~~ belongs (belong) to at least one of the following families of active substances: is selected from the group consisting of: antilucer drugs, antidiabetics, anticoagulants, antithrombics, hypolipidaemics, antiarrhythmics, vasodilators, antiangina drugs, antihypertensives, vasoprotectors, fertility promoters, labour inducers and inhibitors, contraceptives, antibiotics, antitifingals, antivirals, anticancer drugs, anti-inflammatories, analgesics, antiepileptics, antiparkinsonism drugs, neuroleptics, hypnotics, anxiolytics, psychostimulants, antimigraine drugs, antidepressants, antitussives, antihistamines, and antiallergics; and wherein none of the at least one active principle(s) is amoxicillin.

18. (Currently Amended) ~~The suspension~~ Suspension according to claim 17, ~~characterized in that the AP wherein at least one of the at least one active principle(s) is selected from the following compounds~~ group consisting of: pentoxifylline, prazosin, aciclovir, nifedipine, diltiazem, naproxen, ibuprofen, flurbiprofen, ketoprofen, fenoprofen, indomethacin, diclofenac, fentiazac, oestradiol valerate, metoprolol, sulpiride, captopril, cimetidine, zidovudine, nicardipine, terfenadine, atenolol, salbutamol, carbamazepine, ranitidine, enalapril, simvastatin, fluoxetine, alprazolam, famotidine, ganciclovir, famciclovir, spirinolactone, 5-asa, quinidine, perindopril, morphine, pentazocine, metformin, paracetamol, omeprazole, metoclopramide, atenolol, salbutamol morphine, verapamil, erythromycin, caffeine, furosemide,

cephalosporins, montelukast, valaciclovir, ascorbic acid salts, diazepam, theophylline, ciprofloxacin, vancomycin, aminoglycosides, penicillins (~~except for amoxicillin~~) and mixtures thereof; and wherein none of the at least one active principle(s) is amoxicillin.

19. (Currently Amended) ~~Drug~~; A drug comprising ~~characterized in that it comprises~~ a suspension according to ~~any one of claims~~ claim 1 to 18.

20. (Currently Amended) ~~Drug, characterized in that it comprises a~~ kit for preparing the suspension according to ~~any one of claims~~ claim 1 [[to 18]], wherein said kit containing comprises:

[[~~-~~]]microcapsules in substantially dry form ~~containing comprising~~ the active principle(s) for saturating the liquid phase with active principle(s) once the [[two]] solid form and liquid phase[[s]] have been brought into contact;

[[~~-~~]]~~and/or~~ a mixture of microcapsules in substantially dry form containing the active principle(s) in the dose that is just necessary for modified release, together with immediate-release uncoated active principle(s) in a necessary and sufficient dose to saturate the liquid phase with active principle(s) once the saturation dose of active principle(s) and the liquid phase have been brought into contact;

[[~~-~~]]~~and~~ the liquid phase;

~~and/or~~ at least part of the ingredients useful for its preparation;[[~~-~~]] ~~and/or~~ the protocol for preparation of the suspension; or combinations thereof.

21. (New) The suspension according to claim 4, wherein said suspension comprises 60 to 85% by weight of liquid phase.

22. (New) The suspension according to claim 4, wherein said suspension comprises 15 to 40% by weight of microcapsules.



23. (New) The suspension according to claim 1, wherein the proportion of dissolved active principle(s) originating from the microcapsules is less than or equal to 5% by weight of the total weight of the active principle(s) contained in the microcapsules.

24. (New) The suspension according to claim 1 wherein the microcapsules have a particle size of between 200 and 800 microns.

25. (New) The suspension according to claim 1 wherein the microcapsules have a particle size of between 200 and 600 microns.

26. (New) The suspension according to claim 1 wherein from 5 to 40% of the total weight of the coated microcapsules is film coating.

27. (New) The suspension according to claim 11, wherein the proportion PI of active principle(s) released during the first 15 minutes of the dissolution test is such that:  $PI \leq 5$  and the remaining active principle(s) is (are) released over a period such that the release time of 50% by weight of AP ( $t_{1/2}$ ) is defined as follows (in hours):  $0.5 \leq t_{1/2} \leq 20$ .